Wound healing and infection in surgery. The clinical impact of smoking and smoking cessation: a systematic review and meta-analysis

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CRD summary
The authors concluded that across all specialties smokers had a higher incidence of post-surgical healing complications than nonsmokers and former smokers had a lifetime higher risk than never smokers. Possible error and bias during the review process and poor quality of the cohort studies means the reliability of the authors conclusions is uncertain.

Authors' objectives
To evaluate the association between smoking and healing complications across all surgical specialties and the effect of perioperative smoking cessation on postoperative healing outcomes.

Searching
MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched to May 2010 for cohort studies and to January 2011 for randomised controlled trials. Search terms were reported. Reference lists of retrieved articles were searched.

Study selection
Cohort studies that assessed healing complications in at least 100 patients (smokers and former smokers) were eligible for inclusion. Randomised controlled trials (RCTs) with at least one week’s treatment that assessed the effect of perioperative smoking cessation on postoperative healing complications were also eligible. Trials with more than 40% drop-out were excluded.

Eligible outcomes included all types of adverse healing events after surgical procedures with access through a skin incision, short-term healing outcomes (wound and tissue flap necrosis, healing delay, dehiscence of wounds and sutured tissue, surgical site infections, non-specified wound complications) and long-term healing outcomes (hernias and lack of fistula or bone healing).

The included RCTs assessed nurse- or surgeon-provided counselling given between two and eight weeks prior to surgery and for up to 30 days after. Operations were elective orthopaedic operations (hip and knee arthroplasty) and general surgical operations (herniotomy, cholecystectomy and colorectal resection). Control interventions ranged from standard advice about smoking and surgical outcomes to a request to maintain daily smoking habits during the perioperative period. All trials assessed self-reported smoking or abstinence and used biochemical validation. The included cohort studies covered all surgical specialties. Twenty-six studies reported complications in former smokers (most compared former with current and never smokers); where reported, former smokers were those abstinent from smoking for a median of four weeks (range two to 52) before surgery.

The author did not report how studies were selected for the review.

Assessment of study quality
The quality of the cohort studies was evaluated using a domain-based evaluation process and the Newcastle-Ottawa Scale scoring checklist to assign a maximum score of 9 for patient selection characteristics, exposure ascertainment, comparability and outcome assessment. The quality of the RCTs was assessed using the Cochrane risk of bias assessment tool and the Jadad scale (maximum possible score 6).

The author did not report how many reviewers performed the quality assessment.

Data extraction
Crude incidence rates or adjusted odds ratios (ORs) were extracted for healing complications.

The author did not report how many reviewers performed data extraction.
Methods of synthesis
Unadjusted and adjusted estimates of pooled outcomes were calculated by the Mantel-Haenszel and inverse variance methods. Analyses of cohort studies compared smokers with nonsmokers for each type of healing complication and former smokers compared with current or never smokers for a combined complication outcome. Statistical heterogeneity was measured with the $I^2$ statistic. Cohort studies were pooled with a random-effects model regardless of the level of heterogeneity; RCTs were pooled using a fixed-effect model where $I^2$ was less than 40%. Odds ratios (OR) and 95% confidence intervals (CI) were reported.

Sensitivity analyses for cohort studies were conducted across complication type, including cohort studies with a maximum Newcastle-Ottawa Scale score and more than 1,000 patients. Sensitivity analyses for RCTs were performed by type of healing complication. Publication bias was assessed using funnel plots if more than 10 studies reported an outcome.

Results of the review
There were 140 cohort studies (479,150 participants) and four RCTs (477 participants). There was considerable clinical heterogeneity in the cohort studies. Various methodological flaws including retrospective data collection, no reporting of missing data, inadequate outcome definition, inadequate post discharge follow-up reporting and inadequate confounder control. All RCTs had a low risk of bias and achieved a maximum Jadad score.

**RCTs:** In four trials, smoking cessation intervention significantly reduced surgical site infections (OR 0.40, 95% CI 0.20 to 0.83) but no other healing complications.

**Cohort studies:** Compared to nonsmokers, smokers had significantly increased odds of necrosis of wounds and tissue flaps (OR 3.60, 95% CI 2.62 to 4.93; nine studies), healing delay and dehiscence (OR 2.07, 95% CI 1.53 to 2.81; 12 studies), surgical site infection (OR 1.79, 95% CI 1.57 to 2.04; 32 studies), unspecified wound complications (OR 2.27, 95% CI 1.82 to 2.84; 17 studies), hernia (OR 2.07, 95% CI 1.23 to 3.47; seven studies) and lack of fistula or bone healing (OR 2.44, 95% CI 1.66 to 3.58; four studies).

For all healing complications combined, former smokers had increased odds of a complication compared with never smokers (OR 1.31, 95% CI 1.10 to 1.56; 15 studies) and reduced odds compared with current smokers (OR 0.28, 95% CI 0.12 to 0.72; two studies).

Sensitivity analyses of only studies with a maximum quality score and more than 1,000 patients showed similar results for smokers versus nonsmokers but a non-significant result for former versus never smokers.

There was some evidence of publication bias for the outcomes of surgical site infection and wound complications in the cohort studies.

Authors’ conclusions
Across all surgical specialties, smokers had a higher incidence of infectious and noninfectious healing complications after surgery compared with nonsmokers. Former smokers appeared to have a lifetime higher risk of healing complications compared with never smokers. Smoking cessation for at least four weeks before surgery reduced surgical site infections but not other healing complications.

CRD commentary
This review specified clear inclusion criteria for study design, intervention, participants and outcomes. Three databases were searched. It was unclear whether there were any language restrictions so the risk of language bias was unknown. Publication bias was assessed for the cohort studies and some evidence was found for two outcomes. It appeared that studies were selected, quality assessed and data extracted by one author so bias and error could not be ruled out. Appropriate quality assessment tools were used and study quality was discussed but results were not reported in full for each study.

Possible error and bias during the review process and poor quality of the cohort studies means the reliability of the authors conclusions is uncertain.
Implications of the review for practice and research

Practice: The authors stated that patients should be encouraged to stop smoking for at least four weeks before surgery to reduce the risk of surgical site infections.

Research: The authors stated a need for more cohort studies to assess the risk of postoperative healing complications for former smokers. Information from a detailed smoking history including abstinence periods should be included in future clinical database studies on surgical outcome. Large multicentre cluster randomised trials were needed to assess the impact of perioperative smoking cessation on healing outcomes.

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